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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/516,444	02/29/2000	Patricia A. Billing-Medel	5995.US.P2	1768

23492 7590 06/30/2004

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EXAMINER	
YAEN, CHRISTOPHER H	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 06/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/516,444	BILLING-MEDEL ET AL.	
	Examiner	Art Unit	
	Christopher H Yaen	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *3-5,7 and 9-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6 and 8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

RE: Billing-Mendel *et al*
Priority Date: 31 October 1996

Election/Restrictions

1. Applicant's election without traverse of group I (claims 1,2, 6, and 8) in Paper No. 11032003 is acknowledged.

2. Claims 1-24 are pending, claims 3-5, 7, 9-24 are withdrawn from further consideration as being drawn to a non-elected invention.

3. Claims 1,2,6, and 8 are examined on the merits.

Information Disclosure Statement

4. The Information Disclosure Statement filed 6/02/2000 & 4/22/2002 (paper no. 622000 & 4222002) is acknowledged and considered. A signed copy of the IDS is attached hereto.

Specification

5. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see page 21). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

6. Claims 1,2,6, and 8 are objected to because of the following informalities: claims recite the term BU106, it is noted in an interview summary 9/18/2002 that applicant's

representative indicated that BU106 was in error and that the term BS106, which is found throughout the specification, was intended. FOR THE PURPOSES OF EXAMINATION, BU106 WILL BE READ AS BS106.

In addition, in the restriction requirement mailed 10/02/2003, it was indicated that upon election of group I, the election of a single sequence and corrections to the claims to indicate the elected sequence was required. The claims as currently recited still read on non-elected sequences. For examination purposes, the claims will be examined to the extent that they read on SEQ ID No: 26. Appropriate correction is required.

7. Claim 1 is also objected to because claim 1 recites "at least other polypeptide", which is grammatically incorrect. Applicant is required to make the appropriate corrections.

Claim Rejections - 35 USC § 101

8. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

9. Claims 1,2,6, and 8 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility.

The disclosed utilities for the MPA comprising at least one BS106 polypeptide, wherein said BS106 is at least 50% identical to that of SEQ ID No: 26, and another protein, include the detection of BS106 in diseases, methods of making antibodies, drug development and screening, and immunoassays. However, neither the specification nor any art of record teaches what the MPA is, how it functions, or a specific and well-established utility for the protein/polypeptide claimed. Moreover, the BS106 polypeptide

that is comprised within the MPA has also not been taught. Furthermore, the specification does not teach a relationship between MPA or BS106 to any specific disease or establish any involvement in the etiology of any specific disease. The asserted utility of the MPA or BS106 polypeptide is based on its discovery as a breast tissue specific protein. However, the specification has not established with any certainty that the claimed MPA is expressed in any specific breast disease. Moreover, one of skill in the art cannot extrapolate from the findings of Table 1, although drawn to the mRNA analysis, how the instantly claimed protein can be used in the detection of breast cancer, based on the fact that the gene is found in both normal and malignant breast samples. Even if there was a differential expression between normal and malignant breast tissue samples, the specification has not taught one of skill in the art that the claimed MPA or BS106 protein is expressed. One of skill in the art would not be able to predict if SEQ ID NO: 26 is translated into a polypeptide expression product, or even if translated, whether its expression has substantially utility.

It is well known in the art that regulation of mRNA translation is one of the major regulatory steps in the control of gene expression (Jansen, M et al, 1995, Pediatric Res, 37 (6): 681-686). Those of skill in the art recognize that expression of mRNA, specific for a tissue type, does not dictate nor predict the translation of such mRNA into a polypeptide. For example, Alberts et al. (Molecular Biology of the Cell, 3rd edition, 1994, page 465) teach that translation of ferritin mRNA into ferritin polypeptide is blocked during periods of iron starvation. Likewise, if excess iron is available, the transferrin receptor mRNA is degraded and no transferrin receptor polypeptide is translated. Many

other proteins are regulated at the translational level rather than the transcriptional level. For instance, Shantz and Pegg (Int J of Biochem and Cell Biol., 1999, Vol. 31, pp. 107-122) teach that ornithine decarboxylase is highly regulated in the cell at the level of translation and that translation of ornithine decarboxylase mRNA is dependent on the secondary structure of the mRNA and the availability of eIF-4E, which mediates translation initiation. McClean and Hill (Eur J of Cancer, 1993, vol. 29A, pp. 2243-2248) teach that p-glycoprotein can be overexpressed in CHO cells following exposure to radiation, without any concomitant overexpression of the p-glycoprotein mRNA. In addition, Fu et al (EMBO Journal, 1996, Vol. 15, pp. 4392-4401) teach that levels of p53 protein expression do not correlate with levels of p53 mRNA levels in blast cells taken from patients with acute myelogenous leukemia, said patients being without mutations in the p53 gene. Yokota, J et al (Oncogene, 1988,Vol.3, pp. 471-475) teach that the retinoblasma (RB) 115 kD protein is not detected in all nine cases of lung small-cell carcinoma, with either normal or abnormal size mRNA, whereas the RB protein is detected in three of four adenocarcinomas and all three squamous cell carcinomas and one of two large cell carcinomas expressing normal size RB mRNA. Thus, predictability of protein translation or the extent of translation is not solely contingent on mRNA expression due to the multitude of homeostatic factors affecting transcription and translation. For the above reasons, one of skill in the art would not be able to predict if SEQ ID NO: 26 or polypeptides that are 50% identical to SEQ ID No: 26 are translated into a polypeptide expression product, or even if translated, whether they are over-expressed.

Given the teachings of unpredictability associated with protein expression and the lack of endogenous protein expression data of MPA or BS106 in the specification, one of skill in the art cannot with any certainty correlate the teachings of the instant specification with any specific disease diagnosis. Because the specification has only provided an expression profile of the BS106 gene and, and artificial expression of the BS106 gene in cell lines and has not taught how the instantly claimed protein functions, what its cellular role is, and what specific or substantial use the claimed polypeptide would have. As such, the specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the disclosed polypeptide and fragments thereof. Because the claimed invention is not supported by a specific asserted utility for the reasons set forth, credibility of any utility cannot be assessed.

Claims 1,2,6 and 8 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112, 1st paragraph

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1,2,6, and 8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case has only set forth a BS106 polypeptide with an amino acid sequence of SEQ ID No: 26 and therefore the written description in this case is not commensurate in scope with the claims that read on a multimeric polypeptide antigen (MPA) comprising a polypeptide, having at least 50% identity to BS106 (SEQ ID No: 26), and another polypeptide.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

What are allelic variants? Reiger et al (Glossary of Genetics and Cytogenetics, Classical and Molecular, 4th Ed., Springer-Verlay, Berlin, 1976) clearly define alleles as one of two or more alternative forms of a gene occupying the same locus on a particular chromosome..... and differing from other alleles of that locus at one or more mutational sites (page 17). Thus, the structure of naturally occurring allelic sequences are not defined, nor in this case, is the structure of allelic variant proteins encoded by allelic variant genes defined. With the exception of SEQ ID NO: 26, the skilled artisan cannot envision the detailed structure of the encompassed polypeptides and or encoded

variants and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The amino acid sequence itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016. Although these court findings are drawn to DNA art, the findings are clearly applicable to the claimed proteins.

Furthermore, although drawn specifically drawn to the DNA art the findings of *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412) are clearly applicable to the instant rejection. The court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Support for allelic variants is provided in the specification on page 17 lines 27-31 where it is disclosed that the polypeptide sequence has at least about 50% identity,

preferably about 60% identity, more preferably about 75-85% identity, and most preferably about 90-95% or more identity to a BS 106 amino acid sequence. However, no disclosure, beyond the mere mention of variants is made in the specification. This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Furthermore, the claims are drawn to an MPA polypeptide that comprises at least one BS106 polypeptide, wherein the BS106 polypeptide is at least 50% identical to that of SEQ ID No: 26, and another polypeptide together forming a protein of 200 kDa. The specification teaches the identification of a breast tissue specific gene termed BS106, however, neither the specification nor the art at the time the invention was filed taught any functional characteristics that one of skill in the art could use to help in the identification of the claimed invention. Because there is a lack of a clear definition and functional characterization of the MPA in the specification, one of skill in the art would not be able to determine whether the inventors of the instant application were in possession of all MPAs comprising a BS106 polypeptide, having at least 50% identity to SEQ ID No: 26, and another protein because it is unclear whether the BS106 polypeptide alone or the association of the BS106 polypeptide with the "other protein" is critical to the functionality of the MPA. Because the claimed MPA and the BS106 protein have not been ascribed with a particular function, one of skill would not be able to readily screen for such compounds, nor would they know that the inventors were entitled the entire scope of MPA claimed.

Therefore only a BS106 polypeptide molecule having an amino acid sequence of SEQ ID No: 26 meets the written description provision of 35 USC 112, first paragraph.

Conclusion

12. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone number for the organization where this application or proceeding is assigned is 703-308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen
Art Unit 1642
December 16, 2003

GARY NICKOL
PRIMARY EXAMINER